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NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	8	JAN 30	Saved answer limit increased
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NEWS	10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
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NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
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NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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NEWS IPC8	For general information regarding STN implementation of IPC 8

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FILE 'BIOSIS' ENTERED AT 08:12:45 ON 10 MAY 2006
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=> "recombinant vaccinia"
L1        4626 "RECOMBINANT VACCINIA"

=> "HCV E1 envelope protein"
L2           3 "HCV E1 ENVELOPE PROTEIN"

=> "HCV envelope"
L3         370 "HCV ENVELOPE"

=> L1 and L3
L4           5 L1 AND L3

=> vector
L5      408152 VECTOR

=> recombinant
L6      384017 RECOMBINANT

=> L3 and L6
L7          77 L3 AND L6

=> L5 and L7
L8          22 L5 AND L7

=> D L4 IBIB ABS 1-5

L4   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        1998:313394  CAPLUS
DOCUMENT NUMBER:         129:107767
TITLE:                   Isolation and characterization of human monoclonal
                         antibodies against hepatitis C virus envelope
                         glycoproteins
AUTHOR(S):               Da Silva Cardoso, Marcia; Siemoneit, Karl; Sturm,
                         Daniela; Krone, Christoph; Moradpour, Darius; Kubanek,
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Bernhard
CORPORATE SOURCE: Blood Transfusion Service of Baden-Wurttemberg and Department of Transfusion Medicine, University of Ulm, Germany
SOURCE: Journal of Medical Virology (1998), 55(1), 28-34
CODEN: JMVIDB; ISSN: 0146-6615
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The isolation and characterization of human monoclonal antibodies (humAbs) against the hepatitis C virus (HCV) glycoproteins E1 and E2 are described. B-cells from blood donors with anti-HCV were transformed with Epstein-Barr virus. The supernatants of the resulting lymphoblastoid clones were screened by ELISA with an extract of cells infected with a **recombinant vaccinia** virus RMPA95 expressing the envelope proteins E1 and E2 of an HCV genotype 1a virus (H strain). Pos. clones were fused to the heteromyeloma cell line K6H6/B5. Fifteen heterohybridoma cell lines have been established. The specificity of the isolated humAbs was determined both by ELISA and Western blot assays. Several recombinant exts. expressing either the E1 or E2 protein or truncated forms were used in an attempt to map the epitopes on the viral glycoproteins. Some of the humAbs were used successfully for immunofluorescence investigation of transfected cells. Seven specific anti-E2 humAbs, which react with the envelope protein 2 of genotype 1a and 1b isolates, were characterized.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:215333 CAPLUS
DOCUMENT NUMBER: 120:215333
TITLE: Immunoassays for anti-hepatitis C virus (HCV) antibodies using antigens with conformational epitopes
INVENTOR(S): Chien, David Y.
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9401778	A1	19940120	WO 1993-US6309	19930702
W: AU, CA, CZ, FI, HU, JP, NO, PL, RU, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346629	A1	19940131	AU 1993-46629	19930702
AU 685059	B2	19980115		
EP 649537	A1	19950426	EP 1993-916942	19930702
EP 649537	B1	20020424		
EP 649537	B2	20060222		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07509060	T2	19951005	JP 1994-503440	19930702
JP 3490085	B2	20040126		
HU 70473	A2	19951030	HU 1995-8	19930702
PL 174686	B1	19980831	PL 1993-307178	19930702
RU 2126158	C1	19990210	RU 1994-46284	19930702
AT 216779	E	20020515	AT 1993-916942	19930702
ES 2171414	T3	20020916	ES 1993-916942	19930702
PT 649537	T	20020930	PT 1993-916942	19930702
CA 2139645	C	20030211	CA 1993-2139645	19930702
CZ 291951	B6	20030618	CZ 1995-6	19930702
JP 2003329687	A2	20031119	JP 2003-109573	19930702
SK 284556	B6	20050602	SK 1995-4	19930702
NO 9500006	A	19950224	NO 1995-6	19950102
FI 9500002	A	19950227	FI 1995-2	19950102
US 2002150883	A1	20021017	US 2001-920879	20010802
PRIORITY APPLN. INFO.:			US 1992-910759 A	19920707

JP 1994-503440	A3	19930702
WO 1993-US6309	A	19930702
US 1994-334460	A1	19941104

AB Immunoassay methods utilizing **HCV envelope** antigens that contain conformational epitopes reactive with antibodies in serum from infected individuals are useful for screening and diagnosis. These antigens detect antibodies that are not detected by denatured **HCV envelope** antigens. In addition, these **HCV envelope** antigens comprised of conformational epitopes are more immunol. reactive than a number of other HCV antigens. This is the first evidence that conformational epitopes may be involved in the immunol. response to HCV antigens. Preparation of E1 and E2 envelope antigens with **recombinant vaccinia** virus is also shown.

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:4188 CAPLUS
DOCUMENT NUMBER: 120:4188
TITLE: Characterization of hepatitis C virus envelope glycoprotein complexes expressed by **recombinant vaccinia** viruses
AUTHOR(S): Ralston, Robert; Thudium, Kent; Berger, Kim; Kuo, Carol; Gervase, Barbara; Hall, John; Selby, Mark; Kuo, George; Houghton, Michael; Choo, Qui Lim
CORPORATE SOURCE: Chiron Corp., Emeryville, CA, 94608, USA
SOURCE: Journal of Virology (1993), 67(11), 6753-61
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors constructed **recombinant vaccinia** virus vectors for expression of the structural region of hepatitis C virus (HCV). Infection of mammalian cells with a vector (vv/HCV1-906) encoding C-E1-E2-NS2 generated major protein species of 22 kDa (C), 33 to 35 kDa (E1), and 70 to 72 kDa (E2), as observed previously with other mammalian expression systems. The bulk of the E1 and E2 expressed by vv/HCV1-906 was integrated into endoplasmic reticulum membranes as core-glycosylated species, suggesting that these E1 and E2 species represent intracellular forms of the **HCV envelope** proteins. HCV E1 and E2 formed E1-E2 complexes which were precipitated by either anti-E1 or anti-E2 serum and which sedimented at approx. 15 S on glycerol d. gradients. No evidence of intermol. disulfide bonding between E1 and E2 was detected. E1 and E2 were copurified to approx. 90% purity by mild detergent extraction, followed by chromatog. on Galanthus nivalus lectin-agarose and DEAE-Fractogel. Immunization of chimpanzees with purified E1-E2 generated high titers of anti-E1 and anti-E2 antibodies. Further studies demonstrated that purified E1-E2 complexes were recognized at high frequency by HCV+ human sera and generated protective immunity in chimpanzees, suggesting that these purified **HCV envelope** proteins display native HCV epitopes.

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:528131 CAPLUS
DOCUMENT NUMBER: 117:128131
TITLE: Hepatitis C virus asialoglycoproteins manufacture for vaccines or immunoassay
INVENTOR(S): Ralston, Robert O.; Marcus, Frank; Thudium, Kent B.; Gervase, Barbara A.; Hall, John A.
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208734	A1	19920529	WO 1991-US8272	19911107
W: AU, CA, CS, FI, HU, JP, NO, PL, RO, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				

EP	414475	A1	19910227	EP 1990-309120	19900821
EP	414475	B1	19971210		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT	161041	E	19971215	AT 1990-309120	19900821
ES	2110411	T3	19980216	ES 1990-309120	19900821
CA	2064705	AA	19910226	CA 1990-2064705	19900822
CA	2064705	C	19990406		
WO	9102820	A1	19910307	WO 1990-US4766	19900822
	W: AU, CA, JP				
AU	9063449	A1	19910403	AU 1990-63449	19900822
AU	655156	B2	19941208		
JP	05502156	T2	19930422	JP 1990-512531	19900822
JP	2001314192	A2	20011113	JP 2001-75114	19900822
WO	9115771	A1	19911017	WO 1991-US2225	19910329
	W: AU, BB, BG, BR, CA, FI, GB, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU				
	RW: BF, BJ, CF, CG, CM, GA, ML, MR, SN, TD, TG				
AU	9176510	A1	19911030	AU 1991-76510	19910329
AU	639560	B2	19930729		
GB	2257784	A1	19930120	GB 1992-20480	19910329
BR	9106309	A	19930420	BR 1991-6309	19910329
HU	62706	A2	19930528	HU 1992-3146	19910329
HU	217025	B	19991129		
JP	05508219	T2	19931118	JP 1991-507636	19910329
JP	2733138	B2	19980330		
RO	109916	B1	19950728	RO 1975-92012	19910329
PL	172133	B1	19970829	PL 1991-296329	19910329
RU	2130969	C1	19990527	RU 1991-5053084	19910329
EP	450931	A1	19911009	EP 1991-302910	19910403
EP	450931	B1	19960612		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP	693687	A1	19960124	EP 1995-114016	19910403
EP	693687	B1	19990728		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT	139343	E	19960615	AT 1991-302910	19910403
ES	2088465	T3	19960816	ES 1991-302910	19910403
AT	182684	E	19990815	AT 1995-114016	19910403
ES	2134388	T3	19991001	ES 1995-114016	19910403
CA	2095521	AA	19920509	CA 1991-2095521	19911107
AU	9190267	A1	19920611	AU 1991-90267	19911107
AU	668078	B2	19960426		
EP	556292	A1	19930825	EP 1992-900091	19911107
EP	556292	B1	19991229		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP	06504431	T2	19940526	JP 1992-500944	19911107
HU	66063	A2	19940928	HU 1993-1336	19911107
EP	842947	A2	19980520	EP 1997-120661	19911107
EP	842947	A3	20011212		
EP	842947	B1	20040421		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
RU	2123528	C1	19981220	RU 1993-43621	19911107
PL	175610	B1	19990129	PL 1991-300038	19911107
AT	188220	E	20000115	AT 1992-900091	19911107
ES	2139591	T3	20000216	ES 1992-900091	19911107
RO	115446	B1	20000228	RO 1993-626	19911107
CA	2203443	C	20010828	CA 1991-2203443	19911107
JP	2001286290	A2	20011016	JP 2001-59335	19911107
CZ	289006	B6	20011017	CZ 1993-824	19911107
RU	2175657	C2	20011110	RU 1997-115378	19911107
JP	2003093081	A2	20030402	JP 2002-199317	19911107
JP	2003174875	A2	20030624	JP 2002-353148	19911107
EP	1471073	A2	20041027	EP 2004-76119	19911107
EP	1471073	A3	20041201		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI	106317	B1	20010115	FI 1992-4349	19920928
NO	9203839	A	19921119	NO 1992-3839	19921001
NO	310241	B1	20010611		
FI	107803	B1	20011015	FI 1993-2025	19930505
NO	9301680	A	19930628	NO 1993-1680	19930507

NO 304380	B1	19981207			
LV 10344	B	19960220	LV 1993-4381		19930531
US 5679342	A	19971021	US 1993-97853		19930727
LT 3808	B	19960325	LT 1993-1747		19931230
US 5968775	A	19991019	US 1995-438435		19950510
US 5712087	A	19980127	US 1995-440519		19950512
US 6312889	B1	20011106	US 1995-440549		19950512
FI 9701702	A	19970421	FI 1997-1702		19970421
FI 107804	B1	20011015			
NO 9702213	A	19970514	NO 1997-2213		19970514
NO 304381	B1	19981207			
PT 102022	B	20001229	PT 1997-102022		19970626
CZ 289923	B6	20020417	CZ 1997-2196		19970710
JP 11071395	A2	19990316	JP 1998-103178		19980414
JP 3207155	B2	20010910			
GR 3031361	T3	20000131	GR 1999-402455		19990929
GR 3032771	T3	20000630	GR 2000-400473		20000228
JP 2004049235	A2	20040219	JP 2003-180211		20030624
JP 2005187479	A2	20050714	JP 2005-35317		20050210
PRIORITY APPLN. INFO.:			US 1989-398667	A	19890825
			US 1990-611419	A	19901108
			US 1990-611965	A	19901108
			US 1991-758880	A	19910913
			US 1987-122714	B2	19871118
			US 1987-139886	B2	19871230
			US 1988-161072	B2	19880226
			US 1988-191263	B2	19880506
			US 1988-263584	B2	19881026
			US 1988-271450	B2	19881114
			US 1989-325338	B2	19890317
			US 1989-341334	B2	19890420
			US 1989-353896	B2	19890421
			US 1989-355002	B2	19890518
			US 1989-355961	B2	19890518
			US 1989-456637	B2	19891221
			US 1990-504352	A	19900404
			JP 1990-512531	A3	19900822
			JP 2001-75114	A3	19900822
			WO 1990-US4766	A	19900822
			JP 2002-199317	A3	19901108
			WO 1991-US2225	A	19910329
			EP 1991-302910	A3	19910403
			CA 1991-2095521	A3	19911107
			CZ 1993-824	A3	19911107
			EP 1992-900091	A3	19911107
			EP 1997-120661	A3	19911107
			JP 1992-500944	A3	19911107
			JP 1998-103178	A3	19911107
			JP 2001-59335	A3	19911107
			WO 1991-US8272	A	19911107
			US 1992-910760	A3	19920707
			FI 1993-2025	A	19930505
			US 1993-97853	A1	19930727

AB Two hepatitis C virus (**HCV**) **envelope** proteins (E1 and E2) are manufactured without sialylation. Expression of these genes in lower eukaryotes, or in mammalian cells in which terminal glycosylation is blocked, results in proteins similar to native HCV glycoproteins. When isolated by mannose-binding GNA (Galanthus nivalus agglutinin) lectin affinity, the E1 and E2 proteins aggregate into virus-like particles. Cells bearing a mannose receptor or asialoglycoprotein receptor are capable of being infected with HCV and of supporting culturing of the virus. E1 and E2 were produced in HeLa S3 cells inoculated with **recombinant Vaccinia** virus containing HCV gene fragments and purified using a GNA-agarose column.

L4 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:585942 BIOSIS
DOCUMENT NUMBER: PREV199497005312
TITLE: Characterization of hepatitis C virus envelope glycoprotein

complexes expressed by **recombinant vaccinia** viruses.

AUTHOR(S): Ralston, Robert; Thudium, Kent; Berger, Kim; Kuo, Carol; Gervase, Barbara; Hall, John; Selby, Mark; Kuo, George; Houghton, Michael [Reprint author]; Choo, Qui-Lim

CORPORATE SOURCE: Chiron Corporation, 4560 Horton St., Emeryville, CA 94608, USA

SOURCE: Journal of Virology, (1993) Vol. 67, No. 11, pp. 6753-6761. CODEN: JOVIAM. ISSN: 0022-538X.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 28 Dec 1993
Last Updated on STN: 28 Dec 1993

AB We constructed **recombinant vaccinia** virus vectors for expression of the structural region of hepatitis C virus (HCV). Infection of mammalian cells with a vector (vv/HCV-1-906) encoding C-E1-E2-NS2 generated major protein species of 22 kDa (C), 33 to 35 kDa (E1), and 70 to 72 kDa (E2), as observed previously with other mammalian expression systems. The bulk of the E1 and E2 expressed by vv/HCV-1-906 was found integrated into endoplasmic reticulum membranes as core-glycosylated species, suggesting that these E1 and E2 species represent intracellular forms of the **HCV envelope** proteins. HCV E1 and E2 formed E1-E2 complexes which were precipitated by either anti-E1 or anti-E2 serum and which sedimented at approximately 15 S on glycerol density gradients. No-evidence of intermolecular disulfide bonding between E1 and E2 was detected. E1 and E2 were copurified to approximately 90% purity by mild detergent extraction followed by chromatography on Galanthus nivalus lectin-agarose and DEAE-Fractogel. Immunization of chimpanzees with purified E1-E2 generated high titers of anti-E1 and anti-E2 antibodies. Further studies, to be reported separately, demonstrated that purified E1-E2 complexes were recognized at high frequency by HCV+ human sera (D. Y. Chien, Q.-L. Choo, R. Ralston, R. Spaete, M. Tong, M. Houghton, and G. Kuo, Lancet, in press) and generated protective immunity in chimpanzees,-(Q.-L. Choo, G. Kuo, R. Ralston, A. Weiner, D. Chien, G. Van Nest, J. Han, K. Berger, K. Thudium, J. Kansopon, J. McFarland, A. Tabrizi, K. Ching, B. Mass, L. B. Cummins, E. Muchmore, and M. Houghton, submitted for publication), suggesting that these purified **HCV envelope** proteins display native HCV epitopes.

=> D L8 IBIB ABS 1-22

L8 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:77653 CAPLUS

TITLE: Expression of protein fused **HCV envelope** protein E2 with His tag and its implication

AUTHOR(S): Du, Dewei; Jia, Zhansheng; Qin, Hongyan; Sun, Qiang; Liu, Qiuping; Nie, Qinghe; Zhou, Yongxing; Han, Hua

CORPORATE SOURCE: Tangdu Hospital, Fourth Military Medical University, Xi'an, 710038, Peop. Rep. China

SOURCE: Jiefangjun Yixue Zazhi (2004), 29(10), 904-906
CODEN: CFCHBN; ISSN: 0577-7402

PUBLISHER: Jenminjun Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The eukaryotic expression **vector** coding HCV gene E2 fused with His-Tag was constructed and expressed in CHO cells to studying the function of **HCV envelope** protein E2. The gene encoding **HCV envelope** protein E2 was amplified from pBRTM/HCV1-3011, a plasmid containing the cDNA of HCVs ORF, by polymerase chain reaction (PCR) method and cloned into the **vector** pET28(a) containing His-Tag to obtain the fused **HCV envelope** protein E2 gene fused with His-Tag. The fused gene was cloned into pcDNA3.1 to construct the **recombinant** plasmid pcDNA3.1-His-E2, which will express the E2 protein, fused with His tag. This **recombinant** plasmid was transfected into CHO cells by Lipofactamine 2000 reagent. The fused protein was identified by indirect

immunofluorescence (IIF) and Western-blot (WB) methods. The pos. results were obtained when the fused protein of HCV E2 with His-Tag were identified by IIF and WB methods. The eukaryotic expression **vector** pcDNA3.1-His-E2 was constructed successfully and the fused proteins were expressed in cells.

L8 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:980959 CAPLUS
DOCUMENT NUMBER: 143:404156
TITLE: Expression and immunoreactivity of an epitope of HCV in a foreign epitope presenting system
AUTHOR(S): Peng, Mei; Dai, Chang-Bai; Chen, Yuan-Ding
CORPORATE SOURCE: Department of Molecular Biology, Institute of Medical Biology, Chinese Academy of Medical Sciences/Peking Union Medical College, Kunming, 650118, Peop. Rep. China
SOURCE: World Journal of Gastroenterology (2005), 11(22), 3363-3367
CODEN: WJGAF2; ISSN: 1007-9327
PUBLISHER: World Journal of Gastroenterology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AIM: To construct and highly express an epitope of hepatitis C virus (HCV) in a foreign epitope presenting **vector** based on an insect virus, and to study the antigenicity of the epitope. METHODS: The HCV epitope sequence (amino acid residues 315 to 328: EGHRMAWDMMMNWS) of the E1 region was constructed at different positions of a foreign epitope presenting **vector** based on an insect virus, flock house virus (FHV) capsid protein encoding gene as a **vector**, and expressed in E. coli cells. Western blotting and ELISA were used to detect the immunoreactivity of these **recombinant** proteins. RESULTS: The gene encoding of the concerned B-cell epitope of HCV E1 envelope protein was expressed on FHV capsid carrier protein at positions I1 (aa 106), I2 (aa 153) and I3 (aa 305), resp., on the surface of FHV capsid protein. The **recombinant** proteins in this system could be highly expressed in more than 40% of total cell protein of E Coli BL21. All the expressed **recombinant** proteins were in inclusion body form, and showed obvious immunoreactivity by Western blotting. Further purified **recombinant** proteins were detected by indirect ELISA as coating antigen resp. All **recombinant** proteins could still show immunoreactivity. CONCLUSION: The epitope of HCV E1 envelope protein can be highly expressed in FHV carrier system as a chimeric protein with high immunoreactivity. This system has multiple entry sites conferring many possible conformations closer to the native one for a given sequence.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:783479 CAPLUS
DOCUMENT NUMBER: 142:213297
TITLE: Molecular cloning, gene expression and purification of **HCV envelope** glycoprotein E2
AUTHOR(S): Du, Dewei; Jia, Zhansheng; Qin, Hongyan; Liu, Qiuping; Zhou, Yongxing; Han, Hua
CORPORATE SOURCE: Tangdu Hospital, Fourth Military Medical University, Xian, Shanxi Province, 710038, Peop. Rep. China
SOURCE: Shijie Huaren Xiaohua Zazhi (2004), 12(2), 315-318
CODEN: SHXZF2; ISSN: 1009-3079
PUBLISHER: Shijie Weichangbingxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB AIM: To obtain a large amount of HCV E2 protein, and to understand the function of the protein and to prepare the antibody against this protein. METHODS: A 831bp of E2 gene fragment was amplified by PCR method from HCV genome and cloned into pET32a(+) **vector**, an E.coli expression **vector**, to construct a **recombinant** plasmid pET32a-HCVE2. The plasmid was transformed into E.coli BL-21 (DE3) to express E2 protein with IPTG induced. The protein E2 fused with HiS tag expressed in the form of inclusion, was purification by Ni-NTA resin column. The protein E2

fused with His tag was detected by SDS-PAGE electrophoresis and Western blot. RESULTS: A novel protein with mol. weight of Mr 55000 was expressed after induction with IPTG in E.coli. The expressed product showed good reactivity to anti-His tag antibody and the HCV pos. serum. CONCLUSION: Cloning, expression and purification of envelope glycoprotein E2 lay a foundation of further study on HCV E2 protein and the receptors of hepatitis virus C.

L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:765582 CAPLUS
DOCUMENT NUMBER: 142:174856
TITLE: A candidate DNA vaccine elicits HCV specific humoral and cellular immune responses
AUTHOR(S): Zhu, Li-Xin; Liu, Jing; Ye, Ye; Xie, You-Hua; Kong, Yu-Ying; Li, Guang-Di; Wang, Yuan
CORPORATE SOURCE: State Key Laboratory of Molecular Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: World Journal of Gastroenterology (2004), 10(17), 2488-2492
CODEN: WJGAF2; ISSN: 1007-9327
PUBLISHER: World Journal of Gastroenterology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To investigate the immunogenicity of candidate DNA vaccine against hepatitis C virus (HCV) delivered by two plasmids expressing **HCV envelope** protein 1 (E1) and envelope protein 2 (E2) antigens resp. and to study the effect of CpG adjuvant on this candidate vaccine. **Recombinant** plasmids expressing HCV E1 and E2 antigens resp. were used to simultaneously inoculate mice with or without CpG adjuvant. Antisera were then collected and titers of anti-HCV antibodies were analyzed by ELISA. One month after the last injection, animals were sacrificed to prepare single-cell suspension of splenocytes. These cells were subjected to HCV antigen specific proliferation assays and cytokine secretion assays to evaluate the cellular immune responses of the vaccinated animals. Antibody responses to HCV E1 and E2 antigens were detected in vaccinated animals. Animals receiving CpG adjuvant had slightly lower titers of anti-HCV antibodies in the sera, while the splenocytes from these animals showed higher HCV-antigen specific proliferation. Anal. of cytokine secretion from the splenocytes was consistent with the above results. While no antigen-specific IL-4 secretion was detected for all vaccinated animals, HCV antigen-specific INF-γ secretion was detected for the splenocytes of vaccinated animals. CpG adjuvant enhanced the secretion of INF-γ but did not change the profile of IL-4 secretion. Vaccination of mice with plasmids encoding HCV E1 and E2 antigens induces humoral and cellular immune responses. CpG adjuvant significantly enhances the cellular immune response.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:684218 CAPLUS
DOCUMENT NUMBER: 142:315003
TITLE: Liver tissue-specific stable expression of human CD81 molecule
AUTHOR(S): Jia, Shuaizheng; Lu, Liping; Liu, Minxia; Zhan, Linsheng; Wang, Haiping; Wang, Quanli
CORPORATE SOURCE: Institute of Transfusion Medicine, Academy of Military Medical Science, Beijing, 100850, Peop. Rep. China
SOURCE: Xibao Yu Fenzi Mianyixue Zazhi (2003), 19(6), 601-603
CODEN: XFMZFM; ISSN: 1007-8738
PUBLISHER: Xibao Yu Fenzi Mianyixue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB RNA was isolated from human HepG2 cells which could be infected with hepatitis C virus (HCV). RT-PCR was carried out using human CD81 gene-specific primers. Amplified fragments were cloned into pGEM-T

vector. Albumin promoter and enhancer which were liver tissue-specific were ligated to the 5' end of human CD81 gene and SV40 polyA sequence was fused with 3' end of CD81. The fused CD81 gene was inserted into eukaryotic expression **vector** pcDNA3 to construct a **recombinant vector** pcDNA3-Alb p-CD81 which was then transfected into Hepa 1-6 cells through lipofectamine mediation. Human CD81 mRNA transcription and its protein expression were detected by RT-PCR and FACS, resp. Sequence anal. showed that the cloned gene segment was human CD81 gene sequence. After transfection, transcripted human CD81 mRNA was obtained and human CD81 mols. were expressed stably on Hepa 1-6 cells. The obtained pos. cell clones which stably express HCV receptor human CD81 lay the foundation for further study on interactions between **HCV envelope** proteins and human CD81, screening of HCV-infection blocking drugs and development of HCV infection mouse model.

L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:884302 CAPLUS
DOCUMENT NUMBER: 139:63984
TITLE: Expression of Hepatitis C Virus Envelope Proteins with a **Recombinant** Baculovirus Expression System
AUTHOR(S): Tang, Lixia; Xu, Zhikai; Fu, Li; Li, Guangyu; Ren, Junping; Yin, Wen
CORPORATE SOURCE: Department of Medical Microbiology, Fourth Military Medical University, Xi'an, 710032, Peop. Rep. China
SOURCE: Huaxi Yike Daxue Xuebao (2002), 33(2), 179-182
CODEN: HYDXET; ISSN: 0257-7712
PUBLISHER: Huaxi Yike Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The stable expression of envelope proteins of hepatitis C virus in insect host cells and use of expressed envelope proteins for detecting the serums of patients with hepatitis C were studied. The envelope gene of HCV H strain was amplified by PCR and inserted in baculovirus **vector** BacPAK8, and then recombined with linear BacPAK6 DNA in insect cells. The **recombinant** baculoviruses were selected by the plaque assay. The insect cells were infected by the **recombinant** baculoviruses that contained the target gene produced E1, E2 proteins, which were characterized with the immunoblot assay and immunofluorescence and used to determine 35 serum samples of patients with hepatitis C. The relative mol. mass of expressed E1 protein was about 21 x 103 and 33 x 103, and that of E2 about 60 x 103. Detection of immunofluorescence indicated that E1, E2 proteins were localized in the cytoplasm of the infected cells. Four of the 35 sera responded to expressed E1; one of them recognized E2 protein. Three of 9 sera which were HCV RNA pos. by PCR were united to E1, E2. The **HCV envelope** protein can be expressed stably in the insect cells, and expressed E proteins could be used in the serol. anal. of the patients with hepatitis C.

L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:832824 CAPLUS
DOCUMENT NUMBER: 137:351491
TITLE: Production of **recombinant HCV envelope** proteins with expression **vectors** encoding avian lysozyme leader or signal peptide
INVENTOR(S): Sablon, Erwin; Van Broekhoven, Annie; Bosman, Alfons; Depla, Erik; Deschamps, Geert
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 319 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085932	A2	20021031	WO 2002-BE62	20020424
WO 2002085932	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2443740	AA	20021031	CA 2002-2443740	20020424
US 2003108561	A1	20030612	US 2002-128590	20020424
US 2003152940	A1	20030814	US 2002-128587	20020424
US 2003211597	A1	20031113	US 2002-128578	20020424
EP 1381671	A2	20040121	EP 2002-764023	20020424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 529019	A	20040528	NZ 2002-529019	20020424
JP 2004536582	T2	20041209	JP 2002-583458	20020424
BR 2002009033	A	20050111	BR 2002-9033	20020424
CN 1636050	A	20050706	CN 2002-812607	20020424
ZA 2003008277	A	20040708	ZA 2003-8277	20031023
ZA 2003008272	A	20050124	ZA 2003-8272	20031023
ZA 2003008274	A	20050124	ZA 2003-8274	20031023
BG 108373	A	20041230	BG 2003-108373	20031121
PRIORITY APPLN. INFO.:			EP 2001-870088 A	20010424
			US 2001-305604P P	20010717
			WO 2002-BE62 W	20020424

AB The current invention relates to **vectors** and methods for efficient expression of **HCV envelope** proteins in eukaryotic cells. More particularly said **vectors** comprise the coding sequence for an avian lysozyme signal peptide or a functional equivalent thereof joined to a **HCV envelope** protein or a part thereof. Said avian lysozyme signal peptide is efficiently removed when the protein comprising said avian lysozyme signal peptide joined to a **HCV envelope** protein or a part thereof is expressed in a eukaryotic cell. Suitable eukaryotic cells include yeast cells such as Saccharomyces or Hansenula cells.

L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2002:43928 CAPLUS
DOCUMENT NUMBER:	136:277718
TITLE:	Live and Killed Rhabdovirus-Based **Vectors** as Potential Hepatitis C Vaccines
AUTHOR(S):	Siler, Catherine A.; McGettigan, James P.; Dietzschold, Bernhard; Herrine, Steven K.; Dubuisson, Jean; Pomerantz, Roger J.; Schnell, Matthias J.
CORPORATE SOURCE:	The Dorrance H. Hamilton Laboratories, Center for Human Virology, Departments of Biochemistry and Molecular Pharmacology, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE:	Virology (2002), 292(1), 24-34 CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER:	Academic Press
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB A highly attenuated, **recombinant** rabies virus (RV) vaccine strain-based **vector** was utilized as a new immunization strategy to induce humoral and cellular responses against hepatitis C (HCV) glycoprotein E2. The authors showed previously that RV-based **vectors** are able to induce strong immune responses against human immunodeficiency virus type 1 (HIV-1) antigens. Here they constructed and characterized 3 replication-competent RV-based **vectors** expressing either both **HCV envelope** proteins E1 and E2 or a modified version of E2 which lacks 85 amino acids of its C terminus and contains the human CD4 transmembrane domain and the CD4 or RV glycoprotein cytoplasmic domain. All 3 constructs stably expressed the resp. protein(s) as indicated by Western blotting and immunostaining. Moreover, surface expression of HCV E2 resulted in efficient incorporation of the **HCV envelope** protein regardless of the presence

of the RV G cytoplasmic domain, which was described previously as a requirement for incorporation of foreign glycoproteins into RV particles. Killed and purified RV virions containing HCV E2 were highly immunogenic in mice and also proved useful as a diagnostic tool, as indicated by a specific reaction with sera from HCV-infected patients. In addition, RV vaccine vehicles were able to induce cellular responses against HCV E2. Thus, **recombinant** RVs are potentially useful vaccine **vectors** against important human viral diseases. (c) 2002 Academic Press.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:912910 CAPLUS
DOCUMENT NUMBER: 137:104371
TITLE: Secretory expression of different C-terminal truncated HCV E1 proteins in mammalian cells and characterization of the expressed products
AUTHOR(S): Zhu, Jun; Kong, Yuying; Liu, Jing; Zhang, Zuchuan; Wang, Yuan; Li, Guangdi
CORPORATE SOURCE: Institute of Biochemistry and Cell Biology, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (2001), 33(6), 634-640
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Three fragments of **HCV envelope** 1 (E1) with different C-terminal truncation at aa310, aa325, aa340 were cloned into the mammalian expression **vector** pSecTagB. An epitope in the hepatitis B surface antigen, preS1(21-47), were genetically engineered onto the N-terminus of the **recombinant** protein and used as an affinity tag for detection and purification The resulting pSec-preS1-E1t310, pSec-preS1-E1t325, and pSec- preS1-E1t340 were transiently expressed in the HeLa cells and antigenicity, secretory efficiency, and glycosylation type of the **recombinant** E1 proteins were compared. All of the three **recombinant** proteins could be detected by both preS1 monoclonal antibody and E1 polyclonal antiserum. The expression products were secreted and highly mannose-type glycosylated, with S1E1t325 being secreted, indicating the influence of the hydrophobic regions on the secretion of the E1 protein. Three CHO cell lines expressing the proteins, S1E1t310, S1E1t325, and S1E1t340, were established and CHO/pSecS1E1t325 was chosen for further study. The secreted S1E1t325 could be enriched from cell culture medium by the preS1 antibody-coupled Sepharose. The glycosylation anal. indicated the lack of complex glycogen even after the E1 was secreted via Golgi complexes. The established stable cell lines and anti-preS1 affinity method could be utilized to enrich and purify the HCV E1 expressed in mammalian cells, and may be used for further characterization of this protein.

L8 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:48187 CAPLUS
DOCUMENT NUMBER: 132:60088
TITLE: **Recombinant** preparation of human hepatitis C virus proteins in genetically engineered bacteria and use of the proteins
INVENTOR(S): Ye, Linbai; Zheng, Jinrong; Meng, Xiaolin; Xu, Jinping
PATENT ASSIGNEE(S): Wuhan Univ., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 4 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 1175637 A 19980311 CN 1996-119615 19960901
PRIORITY APPLN. INFO.: CN 1996-119615 19960901
AB Described is a method of **recombinant** preparation of hepatitis C virus (**HCV**) **envelope** proteins E1 and E2 and core protein C by expression of the encoding genes in transgenic bacteria such as Escherichia coli strain BL21. The HCV E1-encoding region (cDNA sequence at 897-1467), the HCV E2-encoding region (1379-1847), and the core protein-encoding region (342-915) are cloned into plasmid **vector** pRSET HisA at restriction sites of Pst-EcoR I, EcoR I-Hind III, and EcoR I-Hind II, resp. E. coli strain BL21 transformed with the 3 plasmid **vectors**, resp., expressed E1, E2 and C proteins. The proteins purified with Ni2+-NTA agarose gel column exhibit mol. weight on SDS-PAGE of 26 (E1), 20 (E2), and 26 kDa (C), resp. A mixture of the 3 HCV proteins is used as an antigen for preparation of HCV diagnosis kit.

L8 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:3587 CAPLUS
DOCUMENT NUMBER: 132:277879
TITLE: Effect of immunization in mice with **recombinant** DNA encoding the hepatitis C virus structural protein
AUTHOR(S): Dou, Jun; Liu, Kezhou; Chen, Zhi; Wo, Jianer; He, Nanxiang; Liu, Yong; Zhang, Mingtai; Wang, Xinzhi; Xu, Chenhuai
CORPORATE SOURCE: Dep. Microbiol., Nanjing Railway Med. Coll., Nanjing, 210009, Peop. Rep. China
SOURCE: Chinese Medical Journal (Beijing, English Edition) (1999), 112(11), 1036-1039
CODEN: CMJODS; ISSN: 0366-6999
PUBLISHER: Chinese Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: To explore the possibility and the efficacy of immune responses in mice inoculated with **recombinant** plasmid pCD-HCV, and to lay a foundation for HCV nucleic acid vaccine development in the future. Methods: The gene fragment coding C and E regions of HCV-II (type I b) was inserted into pCD-SRα1 expression **vector** and formed pCD-HCV1 and then was injected into quadriceps muscles of Balb/c mouse. Serum anti-HCV level of mice was tested by ELISA (A value). Spleen cells proliferation responses to HCV antigens were detected by 3H-TdR incorporation (cpm). Results: Balb/c mice immunized with **recombinant** plasmid pCD-HCV1 three or four times can generate specific antibody responses to HCV antigens and the antibody levels gradually ascend to the plateaus and did not have the trend of descending in 18 wk detected. The serum antibodies in mice immunized by **recombinant** plasmid pCD-HCV1 were 100 percent pos. when the serum were diluted 40 times and the pos. rate of antibody still were 16.6 percent pos. when the serum were diluted 320 times. Balb/c mice immunized with **recombinant** plasmid pCD-HCV1 (100 μg, 50 μg, 10 μg/mouse three times resp.) can elicit antibody responses to HCV antigens and the antibody levels of three groups were 0.07 ± 0.07, 0.33 ± 0.04 and 0.11 ± 0.09 resp. Spleen cells Balb/c mice injected with pCD-HCV1 three times were induced to produce proliferation responses to HCVc+e specific antigens. Conclusions: These results demonstrated that constructs expressing HCV core and envelope proteins can generate anti-HCVc+e specific antibody responses and lymphoproliferation responses in mice, which suggested it to be possible to elicit immune responses to viral epitopes from HCV via DNA immunization with HCV-DNA **recombinant** and to warrant further investigation as a potential vaccine against HCV infections.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:731762 CAPLUS
DOCUMENT NUMBER: 131:347494
TITLE: Improved methods for preparing hepatitis C virus envelope glycoproteins E1 and E2/NS1
INVENTOR(S): Min, Mi-Kyung; Park, Joon-Sang; Kim, Jung-Seob; Yun,

Yung-Dae; Moon, Hong-Mo
PATENT ASSIGNEE(S): Mogam Biotechnology Research Institute, S. Korea
SOURCE: U.S., 23 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5985609	A	19991116	US 1994-334545	19941104
PRIORITY APPLN. INFO.:			US 1994-334545	19941104

AB The present invention relates to a novel process for preparing hepatitis C virus (**HCV**) **envelope** glycoproteins employing Chinese Hamster Ovary (CHO) cells transformed with **recombinant** expression **vectors** containing the hepatitis C virus genome. The present invention provides CHO cells cotransfected with DHFR (dihydrofolate reductase) minigene pDCHIP and **recombinant** expression **vectors** containing cDNAs of HCV E1 and E2/NS1 ligated with tissue plasminogen activator signal sequence. HCV E1 and E2/NS1 envelope glycoproteins are produced in a massive manner from the transformed CHO cells adapted in methotrexate. The **HCV envelope** glycoproteins produced by the present invention can be applied to the development of a diagnostic reagent and a potential preventive HCV vaccine.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:592014 CAPLUS
DOCUMENT NUMBER: 129:301407
TITLE: Hepatitis C virus envelope DNA-based immunization elicits humoral and cellular immune responses
AUTHOR(S): Lee, Seung Woo; Cho, Jae Ho; Lee, Ki Jeong; Sung, Young Chul
CORPORATE SOURCE: Department of Life Science, Center for Biofunctional Molecules, School of Environmental Engineering, Pohang University of Science and Technology, Pohang, 790-784, S. Korea
SOURCE: Molecules and Cells (1998), 8(4), 444-451
CODEN: MOCEEK; ISSN: 1016-8478
PUBLISHER: Springer-Verlag Singapore Pte. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The vaccine development for hepatitis C virus (HCV) is highly urgent to prevent non A and non B hepatitis. It was recently shown that the **HCV envelope** proteins appeared to the key viral antigens to induce protective immunity. To generate immune responses to the **HCV envelope** proteins on the DNA-based immunization, various envelope gene-containing plasmids were constructed. For efficient expression and secretion of envelope proteins, the signal sequence of each envelope protein was replaced with either herpes simplex virus type-1 (HSV-1) gD or signal sequence of gD and truncated C-terminal hydrophobic regions of envelope proteins. The i.m. injection of these plasmids generated a significant level of antibody titers to the E1 and E2 proteins, which maximally reached 850 and 25,000 resp. The secreted form of each envelope protein and the fusion of the highly immunogenic gD proteins were shown to have no significant effect on generating immune responses to the envelope proteins. In addition, immunized rats appeared to generate antibodies directed to the homologous HVR-1 peptide. Splenic lymphocytes from immunized rats were shown to induce significant T-cell proliferative responses with the stimulation of **recombinant** E1 and E2 proteins. Our results demonstrated that the **HCV envelope**-DNA based immunization could elicit both humoral and cellular immune responses.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:467599 CAPLUS
DOCUMENT NUMBER: 129:199513
TITLE: Characterization of the structural proteins of hepatitis C virus expressed by an adenovirus **recombinant**
AUTHOR(S): Rim Seong, Young; Lee, Chan-Hee; Im, Dong-Soo
CORPORATE SOURCE: Gene Therapy Research Unit, Korea Research Institute of Bioscience and Biotechnology, Taejeon, S. Korea
SOURCE: Virus Research (1998), 55(2), 177-185
CODEN: VIREDF; ISSN: 0168-1702
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human adenoviruses have been used for mammalian expression **vectors** and **recombinant** vaccines for heterologous antigens. The authors constructed and characterized an infectious adenovirus **recombinant** containing core-E1-E2 genes of hepatitis C virus (HCV). The core protein was produced mainly during the early phase of viral infection. Expression of HCV E1 and E2 envelope proteins was detected by an immunopptn. with HCV-pos. patient's sera. The purified E1 and E2 proteins appeared to be composed of mainly a heterodimeric form via noncovalent interaction, as previously observed in other mammalian expression systems. A small portion of E1 and E2 monomers as well as E1E2 aggregates by inter-disulfide linkage were detected. Apparently heterodimeric E1E2 complexes were serol. reactive. The results suggest that adenovirus is an useful HCV antigen-expression **vector**.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:698698 CAPLUS
DOCUMENT NUMBER: 126:6277
TITLE: Expression of **HCV envelope** proteins and the serological utility of the anti-E2 immune response
AUTHOR(S): Lesniewski, Richard R.; Watanabe, Shinichi; Devare, Sushil G.
CORPORATE SOURCE: Hepatitis Research and Development, Abbott Laboratories, Abbott Park, IL, 60064, USA
SOURCE: Proceedings of the International Symposium of the Princess Takamatsu Cancer Research Fund (1995), Volume Date 1994, 25th(Hepatitis C Virus and Its Involvement in the Development of Hepatocellular Carcinoma), 129-137
CODEN: PPTCBY
PUBLISHER: Princeton Scientific
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5' end of the hepatitis C virus (HCV) genome encodes structural proteins of the virion. The first gene encodes a highly basic core protein. Immediately downstream of the core gene are regions which encode the envelope proteins (E1 and E2) of the virus. Artificial expression and secretion of immunol. active envelope proteins have proven to be a substantial challenge due to the high degree of glycosylation and the existence of certain hydrophobic domains contained within these sequences. Bacterial cell expression of **recombinant HCV envelope** proteins results in products that are not glycosylated and are poorly immunogenic. Emphasis has shifted to the use of mammalian cell lines (human embryonic kidney [HEK] and Chinese hamster ovary [CHO] cells) for the expression of glycosylated, immunol. active envelope proteins. Using HEK cells, E1 is expressed intracellularly but is not secreted from the cells. When E1 is cloned in fusion with a C-terminal truncated E2 protein, both proteins are detected intracellularly; however, only E2 is secreted. When the E1/E2 processing site is interrupted by constructing deletion mutants, the unprocessed E1/E2 fusion protein can be secreted from the cells. Quantifiable expression and secretion of a truncated E2 protein is now possible using CHO cells and SV40-based **vectors**. The HCV E2 glycoprotein expressed from CHO cells is

highly antigenic; a strong humoral response to this antigen develops in persons infected with HCV. Antibodies to E2 are found in 95% of patients with detectable HCV RNA in their sera. The presence of antibodies to E2 is not indicative of viral clearance and therefore the role these antibodies play in protective immunity, if any, is unclear.

L8 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:4188 CAPLUS
DOCUMENT NUMBER: 120:4188
TITLE: Characterization of hepatitis C virus envelope glycoprotein complexes expressed by **recombinant** vaccinia viruses
AUTHOR(S): Ralston, Robert; Thudium, Kent; Berger, Kim; Kuo, Carol; Gervase, Barbara; Hall, John; Selby, Mark; Kuo, George; Houghton, Michael; Choo, Qui Lim
CORPORATE SOURCE: Chiron Corp., Emeryville, CA, 94608, USA
SOURCE: Journal of Virology (1993), 67(11), 6753-61
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors constructed **recombinant** vaccinia virus **vectors** for expression of the structural region of hepatitis C virus (HCV). Infection of mammalian cells with a **vector** (vv/HCV1-906) encoding C-E1-E2-NS2 generated major protein species of 22 kDa (C), 33 to 35 kDa (E1), and 70 to 72 kDa (E2), as observed previously with other mammalian expression systems. The bulk of the E1 and E2 expressed by vv/HCV1-906 was integrated into endoplasmic reticulum membranes as core-glycosylated species, suggesting that these E1 and E2 species represent intracellular forms of the **HCV envelope** proteins. HCV E1 and E2 formed E1-E2 complexes which were precipitated by either anti-E1 or anti-E2 serum and which sedimented at approx. 15 S on glycerol d. gradients. No evidence of intermol. disulfide bonding between E1 and E2 was detected. E1 and E2 were copurified to approx. 90% purity by mild detergent extraction, followed by chromatog. on Galanthus nivalus lectin-agarose and DEAE-Fractogel. Immunization of chimpanzees with purified E1-E2 generated high titers of anti-E1 and anti-E2 antibodies. Further studies demonstrated that purified E1-E2 complexes were recognized at high frequency by HCV+ human sera and generated protective immunity in chimpanzees, suggesting that these purified **HCV envelope** proteins display native HCV epitopes.

L8 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:528131 CAPLUS
DOCUMENT NUMBER: 117:128131
TITLE: Hepatitis C virus asialoglycoproteins manufacture for vaccines or immunoassay
INVENTOR(S): Ralston, Robert O.; Marcus, Frank; Thudium, Kent B.; Gervase, Barbara A.; Hall, John A.
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208734	A1	19920529	WO 1991-US8272	19911107
W: AU, CA, CS, FI, HU, JP, NO, PL, RO, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
EP 414475	A1	19910227	EP 1990-309120	19900821
EP 414475	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 161041	E	19971215	AT 1990-309120	19900821
ES 2110411	T3	19980216	ES 1990-309120	19900821
CA 2064705	AA	19910226	CA 1990-2064705	19900822
CA 2064705	C	19990406		

WO 9102820		A1	19910307	WO 1990-US4766	19900822
W: AU, CA, JP					
AU 9063449		A1	19910403	AU 1990-63449	19900822
AU 655156		B2	19941208		
JP 05502156		T2	19930422	JP 1990-512531	19900822
JP 2001314192		A2	20011113	JP 2001-75114	19900822
WO 9115771		A1	19911017	WO 1991-US2225	19910329
W: AU, BB, BG, BR, CA, FI, GB, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU					
RW: BF, BJ, CF, CG, CM, GA, ML, MR, SN, TD, TG					
AU 9176510		A1	19911030	AU 1991-76510	19910329
AU 639560		B2	19930729		
GB 2257784		A1	19930120	GB 1992-20480	19910329
BR 9106309		A	19930420	BR 1991-6309	19910329
HU 62706		A2	19930528	HU 1992-3146	19910329
HU 217025		B	19991129		
JP 05508219		T2	19931118	JP 1991-507636	19910329
JP 2733138		B2	19980330		
RO 109916		B1	19950728	RO 1975-92012	19910329
PL 172133		B1	19970829	PL 1991-296329	19910329
RU 2130969		C1	19990527	RU 1991-5053084	19910329
EP 450931		A1	19911009	EP 1991-302910	19910403
EP 450931		B1	19960612		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
EP 693687		A1	19960124	EP 1995-114016	19910403
EP 693687		B1	19990728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AT 139343		E	19960615	AT 1991-302910	19910403
ES 2088465		T3	19960816	ES 1991-302910	19910403
AT 182684		E	19990815	AT 1995-114016	19910403
ES 2134388		T3	19991001	ES 1995-114016	19910403
CA 2095521		AA	19920509	CA 1991-2095521	19911107
AU 9190267		A1	19920611	AU 1991-90267	19911107
AU 668078		B2	19960426		
EP 556292		A1	19930825	EP 1992-900091	19911107
EP 556292		B1	19991229		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 06504431		T2	19940526	JP 1992-500944	19911107
HU 66063		A2	19940928	HU 1993-1336	19911107
EP 842947		A2	19980520	EP 1997-120661	19911107
EP 842947		A3	20011212		
EP 842947		B1	20040421		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
RU 2123528		C1	19981220	RU 1993-43621	19911107
PL 175610		B1	19990129	PL 1991-300038	19911107
AT 188220		E	20000115	AT 1992-900091	19911107
ES 2139591		T3	20000216	ES 1992-900091	19911107
RO 115446		B1	20000228	RO 1993-626	19911107
CA 2203443		C	20010828	CA 1991-2203443	19911107
JP 2001286290		A2	20011016	JP 2001-59335	19911107
CZ 289006		B6	20011017	CZ 1993-824	19911107
RU 2175657		C2	20011110	RU 1997-115378	19911107
JP 2003093081		A2	20030402	JP 2002-199317	19911107
JP 2003174875		A2	20030624	JP 2002-353148	19911107
EP 1471073		A2	20041027	EP 2004-76119	19911107
EP 1471073		A3	20041201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
FI 106317		B1	20010115	FI 1992-4349	19920928
NO 9203839		A	19921119	NO 1992-3839	19921001
NO 310241		B1	20010611		
FI 107803		B1	20011015	FI 1993-2025	19930505
NO 9301680		A	19930628	NO 1993-1680	19930507
NO 304380		B1	19981207		
LV 10344		B	19960220	LV 1993-4381	19930531
US 5679342		A	19971021	US 1993-97853	19930727
LT 3808		B	19960325	LT 1993-1747	19931230
US 5968775		A	19991019	US 1995-438435	19950510
US 5712087		A	19980127	US 1995-440519	19950512
US 6312889		B1	20011106	US 1995-440549	19950512

FI 9701702	A	19970421	FI 1997-1702	19970421
FI 107804	B1	20011015		
NO 9702213	A	19970514	NO 1997-2213	19970514
NO 304381	B1	19981207		
PT 102022	B	20001229	PT 1997-102022	19970626
CZ 289923	B6	20020417	CZ 1997-2196	19970710
JP 11071395	A2	19990316	JP 1998-103178	19980414
JP 3207155	B2	20010910		
GR 3031361	T3	20000131	GR 1999-402455	19990929
GR 3032771	T3	20000630	GR 2000-400473	20000228
JP 2004049235	A2	20040219	JP 2003-180211	20030624
JP 2005187479	A2	20050714	JP 2005-35317	20050210

PRIORITY APPLN. INFO.:

US 1989-398667	A	19890825
US 1990-611419	A	19901108
US 1990-611965	A	19901108
US 1991-758880	A	19910913
US 1987-122714	B2	19871118
US 1987-139886	B2	19871230
US 1988-161072	B2	19880226
US 1988-191263	B2	19880506
US 1988-263584	B2	19881026
US 1988-271450	B2	19881114
US 1989-325338	B2	19890317
US 1989-341334	B2	19890420
US 1989-353896	B2	19890421
US 1989-355002	B2	19890518
US 1989-355961	B2	19890518
US 1989-456637	B2	19891221
US 1990-504352	A	19900404
JP 1990-512531	A3	19900822
JP 2001-75114	A3	19900822
WO 1990-US4766	A	19900822
JP 2002-199317	A3	19901108
WO 1991-US2225	A	19910329
EP 1991-302910	A3	19910403
CA 1991-2095521	A3	19911107
CZ 1993-824	A3	19911107
EP 1992-900091	A3	19911107
EP 1997-120661	A3	19911107
JP 1992-500944	A3	19911107
JP 1998-103178	A3	19911107
JP 2001-59335	A3	19911107
WO 1991-US8272	A	19911107
US 1992-910760	A3	19920707
FI 1993-2025	A	19930505
US 1993-97853	A1	19930727

AB Two hepatitis C virus (**HCV**) **envelope** proteins (E1 and E2) are manufactured without sialylation. Expression of these genes in lower eukaryotes, or in mammalian cells in which terminal glycosylation is blocked, results in proteins similar to native HCV glycoproteins. When isolated by mannose-binding GNA (Galanthus nivalus agglutinin) lectin affinity, the E1 and E2 proteins aggregate into virus-like particles. Cells bearing a mannose receptor or asialoglycoprotein receptor are capable of being infected with HCV and of supporting culturing of the virus. E1 and E2 were produced in HeLa S3 cells inoculated with **recombinant** Vaccinia virus containing HCV gene fragments and purified using a GNA-agarose column.

L8 ANSWER 18 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:325626 BIOSIS
DOCUMENT NUMBER: PREV200200325626
TITLE: Expression of hepatitis C virus envelope proteins with a **recombinant** baculovirus expression system.
AUTHOR(S): Tang Lixia [Reprint author]; Xu Zhikai; Fu Li; Li Guangyu; Ren Junping; Yin Wen
CORPORATE SOURCE: Department of Medical Microbiology, Fourth Military Medical University, Xi'an, 710032, China
SOURCE: Journal of West China University of Medical Sciences,

(April, 2002) Vol. 33, No. 2, pp. 179-182. print.
CODEN: HYDXET. ISSN: 0257-7712.
DOCUMENT TYPE: Article
LANGUAGE: Chinese
ENTRY DATE: Entered STN: 5 Jun 2002
Last Updated on STN: 5 Jun 2002

AB Objective To acquire stable expression of envelope proteins of hepatitis C virus in insect host cells and use the expressed envelope proteins for detecting the serums of patients with hepatitis C. Methods The envelope gene of HCV H strain was amplified by PCR and inserted in baculovirus **vector** BacPAK8, and then recombined with linear BacPAK6 DNA in insect cells. The **recombinant** baculoviruses were selected by the plaque assay. The insect cells were infected by the **recombinant** baculoviruses that contained the target gene produced E1, E2 proteins, which were characterized with the immunoblot assay and the immunofluorescence and were used to determine 35 serum samples of patients with hepatitis C. Results The expressed E1, E2 proteins showed that the relative molecular mass of E1 is about 21 X 103 and 33 X 103, and that of E2 is about 60 X 103. Detection of immunofluorescence indicated that E1, E2 proteins are localized in the cytoplasm of the infected cells. Four of the 35 serums responded to expressed E1; one of them was found to recognize E2 protein. Three of 9 serums which were HCV RNA positive by PCR testing got united to E1, E2. Conclusion The **HCV envelope** protein can be expressed stably in the insect cells. Expressed E proteins could be used in the serologic analysis of the patients' serums.

L8 ANSWER 19 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:163564 BIOSIS
DOCUMENT NUMBER: PREV200200163564
TITLE: Live and killed rhabdovirus-based **vectors** as potential hepatitis C vaccines.
AUTHOR(S): Siler, Catherine A.; McGettigan, James P.; Dietzschold, Bernhard; Herrine, Steven K.; Dubuisson, Jean; Pomerantz, Roger J.; Schnell, Matthias J. [Reprint author]
CORPORATE SOURCE: 1020 Locust Street, Suite 335, Philadelphia, PA, 19107-6799, USA
matthias.schnell@mail.tju.edu
SOURCE: Virology, (January 5, 2002) Vol. 292, No. 1, pp. 24-34. print.
CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002

AB A highly attenuated, **recombinant** rabies virus (RV) vaccine strain-based **vector** was utilized as a new immunization strategy to induce humoral and cellular responses against hepatitis C (HCV) glycoprotein E2. We showed previously that RV-based **vectors** are able to induce strong immune responses against human immunodeficiency virus type I (HIV-1) antigens. Here we constructed and characterized three replication-competent RV-based **vectors** expressing either both **HCV envelope** proteins E1 and E2 or a modified version of E2 which lacks 85 amino acids of its carboxy terminus and contains the human CD4 transmembrane domain and the CD4 or RV glycoprotein cytoplasmic domain. All three constructs stably expressed the respective protein(s) as indicated by Western blotting and immunostaining. Moreover, surface expression of HCV E2 resulted in efficient incorporation of the **HCV envelope** protein regardless of the presence of the RV G cytoplasmic domain, which was described previously as a requirement for incorporation of foreign glycoproteins into RV particles. Killed and purified RV virions containing HCV E2 were highly immunogenic in mice and also proved useful as a diagnostic tool, as indicated by a specific reaction with sera from HCV-infected patients. In addition, RV vaccine vehicles were able to induce cellular responses against HCV E2. These results further suggest that **recombinant** RVs are potentially useful vaccine **vectors** against important human viral diseases.

L8 ANSWER 20 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:27506 BIOSIS
DOCUMENT NUMBER: PREV200200027506
TITLE: Secretory expression of different C-terminal truncated HCV E1 proteins in mammalian cells and characterization of the expressed products.
AUTHOR(S): Zhu Jun; Kong Yu-Ying; Liu Jing; Zhang Zu-Chuan; Wang Yuan [Reprint author]; Li Guang-Di [Reprint author]
CORPORATE SOURCE: Institute of Biochemistry and Cell Biology, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, China
wangyuan@server.shcnc.ac.cn
SOURCE: Shengwu Huaxue yu Shengwu Wuli Xuebao, (Nov., 2001) Vol. 33, No. 6, pp. 634-640. print.
ISSN: 0582-9879.
DOCUMENT TYPE: Article
LANGUAGE: Chinese
ENTRY DATE: Entered STN: 26 Dec 2001
Last Updated on STN: 25 Feb 2002

AB Three fragments of the **HCV envelope** 1 (E1) with different C terminal truncation at aa310, aa325, aa340 were cloned into the mammalian expression **vector** pSecTagB. An epitope in the hepatitis B surface antigen, preS1(21-47), were genetically engineered onto the N-terminus of the **recombinant** protein and used as an affinity tag for detection and purification. The resulting pSec-preS1-E1t310, pSec-preS1-E1t325 and pSec-preS1-E1t340 were transiently expressed in the HeLa cells and the antigenicity, secretory efficiency and glycosylation type of the **recombinant** E1 proteins were compared. All of the three **recombinant** proteins could be detected by both preS1 monoclonal antibody and E1 polyclonal antiserum. The expression products were secreted and highly mannose-type glycosylated, with S1E1t325 being secreted, indicating the influence of the hydrophobic regions on the secretion of the E1 protein. Three CHO cell lines expressing the proteins, S1E1t310, S1E1t325 and S1E1t340, were established and the CHO/pSecS1E1t325 was chosen for further study. The secreted S1E1t325 could be enriched from cell culture medium by the preS1 antibody-coupled Sepharose. The glycosylation analysis indicated the lack of complex glycogen even after the E1 was secreted via Golgi complexes. The established stable cell lines and anti-preS1 affinity method could be utilized to enrich and purify the HCV E1 expressed in mammalian cells, and may be used for further characterization of this protein.

L8 ANSWER 21 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:277712 BIOSIS
DOCUMENT NUMBER: PREV200000277712
TITLE: Process for preparing hepatitis C virus envelope glycoproteins.
AUTHOR(S): Min, Mi-Kyung [Inventor, Reprint author]; Park, Joon-Sang [Inventor]; Kim, Jung-Seob [Inventor]; Yun, Yung-Dae [Inventor]; Moon, Hong-Mo [Inventor]
CORPORATE SOURCE: Seoul, North Korea
ASSIGNEE: Mogam Biotechnology Research Institute, Kyonggi-Do, North Korea
PATENT INFORMATION: US 5985609 19991116
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 16, 1999) Vol. 1228, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002

AB The present invention relates to a novel process for preparing hepatitis C virus (**HCV**) **envelope** glycoproteins employing Chinese Hamster Ovary (CHO) cells transformed with **recombinant** expression **vectors** containing the hepatitis C virus genome. The present invention provides CHO cells cotransfected with DHFR (dihydrofolate reductase) minigene pDCHIP and **recombinant**

expression **vectors** containing cDNAs of HCV E1 and E2/NS1 ligated with tissue plasminogen activator signal sequence. HCV E1 and E2/NS1 envelope glycoproteins are produced in a massive manner from the transformed CHO cells adapted in methotrexate. The **HCV envelope** glycoproteins produced by the present invention can be applied to the development of a diagnostic reagent and a potential preventive HCV vaccine.

L8 ANSWER 22 OF 22 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1993:585942 BIOSIS
DOCUMENT NUMBER: PREV199497005312
TITLE: Characterization of hepatitis C virus envelope glycoprotein complexes expressed by **recombinant** vaccinia viruses.
AUTHOR(S): Ralston, Robert; Thudium, Kent; Berger, Kim; Kuo, Carol; Gervase, Barbara; Hall, John; Selby, Mark; Kuo, George; Houghton, Michael [Reprint author]; Choo, Qui-Lim
CORPORATE SOURCE: Chiron Corporation, 4560 Horton St., Emeryville, CA 94608, USA
SOURCE: Journal of Virology, (1993) Vol. 67, No. 11, pp. 6753-6761. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 1993
Last Updated on STN: 28 Dec 1993

AB We constructed **recombinant** vaccinia virus **vectors** for expression of the structural region of hepatitis C virus (HCV). Infection of mammalian cells with a **vector** (vv/HCV-1-906) encoding C-E1-E2-NS2 generated major protein species of 22 kDa (C), 33 to 35 kDa (E1), and 70 to 72 kDa (E2), as observed previously with other mammalian expression systems. The bulk of the E1 and E2 expressed by vv/HCV-1-906 was found integrated into endoplasmic reticulum membranes as core-glycosylated species, suggesting that these E1 and E2 species represent intracellular forms of the **HCV envelope** proteins. HCV E1 and E2 formed E1-E2 complexes which were precipitated by either anti-E1 or anti-E2 serum and which sedimented at approximately 15 S on glycerol density gradients. No-evidence of intermolecular disulfide bonding between E1 and E2 was detected. E1 and E2 were copurified to approximately 90% purity by mild detergent extraction followed by chromatography on Galanthus nivalus lectin-agarose and DEAE-Fractogel. Immunization of chimpanzees with purified E1-E2 generated high titers of anti-E1 and anti-E2 antibodies. Further studies, to be reported separately, demonstrated that purified E1-E2 complexes were recognized at high frequency by HCV+ human sera (D. Y. Chien, Q.-L. Choo, R. Ralston, R. Spaete, M. Tong, M. Houghton, and G. Kuo, Lancet, in press) and generated protective immunity in chimpanzees,-(Q.-L. Choo, G. Kuo, R. Ralston, A. Weiner, D. Chien, G. Van Nest, J. Han, K. Berger, K. Thudium, J. Kansopon, J. McFarland, A. Tabrizi, K. Ching, B. Mass, L. B. Cummins, E. Muchmore, and M. Houghton, submitted for publication), suggesting that these purified **HCV envelope** proteins display native HCV epitopes.

L4 · ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:215333 CAPLUS
DOCUMENT NUMBER: 120:215333
TITLE: Immunoassays for anti-hepatitis C virus (HCV) antibodies using antigens with conformational epitopes
INVENTOR(S): Chien, David Y.
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9401778	A1	19940120	WO 1993-US6309	19930702
W: AU, CA, CZ, FI, HU, JP, NO, PL, RU, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346629	A1	19940131	AU 1993-46629	19930702
AU 685059	B2	19980115		
EP 649537	A1	19950426	EP 1993-916942	19930702
EP 649537	B1	20020424		
EP 649537	B2	20060222		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07509060	T2	19951005	JP 1994-503440	19930702
JP 3490085	B2	20040126		
HU 70473	A2	19951030	HU 1995-8	19930702
PL 174686	B1	19980831	PL 1993-307178	19930702
RU 2126158	C1	19990210	RU 1994-46284	19930702
AT 216779	E	20020515	AT 1993-916942	19930702
ES 2171414	T3	20020916	ES 1993-916942	19930702
PT 649537	T	20020930	PT 1993-916942	19930702
CA 2139645	C	20030211	CA 1993-2139645	19930702
CZ 291951	B6	20030618	CZ 1995-6	19930702
JP 2003329687	A2	20031119	JP 2003-109573	19930702
SK 284556	B6	20050602	SK 1995-4	19930702
NO 9500006	A	19950224	NO 1995-6	19950102
FI 9500002	A	19950227	FI 1995-2	19950102
US 2002150883	A1	20021017	US 2001-920879	20010802

PRIORITY APPLN. INFO.:

US 1992-910759	A	19920707
JP 1994-503440	A3	19930702
WO 1993-US6309	A	19930702
US 1994-334460	A1	19941104

AB Immunoassay methods utilizing **HCV envelope** antigens that contain conformational epitopes reactive with antibodies in serum from infected individuals are useful for screening and diagnosis. These antigens detect antibodies that are not detected by denatured **HCV envelope** antigens. In addition, these **HCV envelope** antigens comprised of conformational epitopes are more immunol. reactive than a number of other HCV antigens. This is the first evidence that conformational epitopes may be involved in the immunol. response to HCV antigens. Preparation of E1 and E2 envelope antigens with **recombinant vaccinia** virus is also shown.